over noradrenaline or whether disadvantages will emerge. It deserves wider trial with a close watch on the renal effect.

Therapy.—The normal indication for giving hypertensin is to raise a lowered blood-pressure to safer levels. Caution is needed with the rate of infusion, and this should not initially exceed 2 μg. per minute, with an increase according to the response. The effect wears off within a minute or two of stopping the infusion. It must not be diluted in blood or plasma, since it is readily destroyed by an enzyme present, and therefore it is always given diluted in a salt or dextrose solution.

Toxicity.—None is known.

N.H.S. Basic Price.—6 × 2 ml. ampoules, 20s.

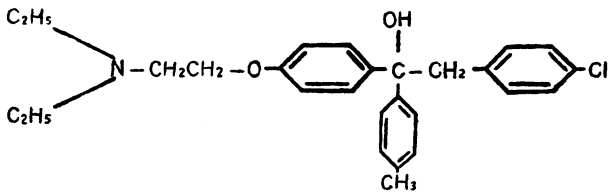
REFERENCES

[1] Elliott, D. F., and Peart, W. S., *Nature (Lond.)*, 1956, **177**, 527.
[2] Skeggs, L. T., Kahn, J. R., Lentz, K. E., Shumway, N. P., and Woods, K. R., *J. exp. Med.*, 1956, **104**, 193.
[3] Schwyzer, R., and Sieber, P., *Chimia*, 1956, **10**, 265.

Triparanol

" Mer-29 " (Merrell-National).

Chemistry. — Triparanol is a synthetic substance structurally related to chlorotrianisene, a synthetic non-steroid oestrogen, and to ethamoxytriphetol, a non-steroid oestrogen antagonist. Chemically it is 1-[4(diethylamino-ethoxy)phenyl]-1-(*p*-tolyl)-2-(*p*-chlorophenyl) ethanol, with the following structural formula:



Pharmacology.—Triparanol inhibits the biosynthesis of cholesterol at a stage in the biosynthetic pathway after the formation of the steroid nucleus, and prevents conversion of the immediate precursor of cholesterol, 24-dehydro-cholesterol or desmosterol, into cholesterol. Consequently, desmosterol appears in the blood in increased quantity, and, since it gives a colour in the Lieberman–Burchard reaction, the reduction of total sterols in the plasma is less than indicated by standard methods of determining cholesterol. Radio-isotope studies have shown, however, that the total sterol pool and the total plasma sterols are decreased by triparanol. Since adrenal steroids and other important steroids, such as progesterone, are synthesized from cholesterol, inhibition of its biosynthesis might theoretically lead to adrenal insufficiency or to a disturbance of ovarian function, but this has apparently not been found during triparanol therapy.

Therapy.—Triparanol is advertised as a practical and safe treatment for hypercholesterolaemia, and there is no doubt that it is effective in reducing the level of plasma cholesterol. Since it causes accumulation of desmosterol, the total plasma sterols are not so strikingly lowered as the plasma cholesterol. Thus, if triparanol is to be used for the reduction of the hypercholesterolaemia often associated with coronary heart disease, a critical question, as yet unanswered, is whether desmosterol is atherogenic. If desmosterol is shown to induce in animals arterial lesions similar to those which result from feeding with cholesterol, then some of the claims for triparanol will have to be modified. A further important comment of a more general nature is that reduction of the plasma cholesterol has not yet been shown to improve the prognosis of patients with coronary heart disease. Thus, while triparanol is effective and non-toxic, its therapeutic value in lowering hypercholesterolaemia has yet to be established.

***Toxicity.*—There** have been fairly extensive clinical trials of triparanol, and at present no serious toxic effects have been reported.

N.H.S. Basic Price.—100 tabs. for 118s. 9d.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Complications of Immunization

SIR,—Under the title " Is Universal Vaccination against Pertussis Always Justified ? " (October 22, p. 1184), Dr. Justus Ström, head of the Hospital for Infectious Diseases, Stockholm, published an article in which he reported a surprisingly high incidence (1 : 6,000) of neurological complications following the injection of Swedish triple-vaccine. The article occasioned in the same issue an annotation (p. 1215) which understandably enough expressed the opinion that " there must be some uneasiness until the reasons for the high complication rate reported from Sweden are known." We feel it is of the utmost concern to bring to notice certain points that should be borne in mind in assessing Dr. Ström's figures.

Routine inoculation of infants with triple-vaccine has been practised in Sweden since the early 1950's, one injection being given at 3, one at 4½, and one at 6 months. The proportion of children treated has steadily increased and has amounted to 60 to 70% of all infants during latter years. The vaccine used is one of those prepared by the State Bacteriological Laboratory, Stockholm, and 1 ml. contains 20,000 to 25,000 million whooping-cough bacteria, 12.5 units diphtheria toxoid, and 7.5 units tetanus toxoid adsorbed on aluminium phosphate. Anaesthetics and preservatives are added. According to the directions, 1 ml. of the vaccine is injected subcutaneously. Its antigenic effect has proved to be extremely good.

Dr. Ström's material dates from the years 1955–8. It represents the answers to a questionary sent out to 64 hospital departments and 693 child-welfare centres. From these answers Dr. Ström has collected 36 neurological cases which he interprets as being due to complications of vaccination, and which vary in severity from rapidly fatal illnesses to isolated attacks of convulsions. The data he provides are extremely scanty, and, as far as we know, he has never himself seen or followed up more than perhaps one or two of all the patients. In 18 of the 36 the symptoms were so slight that specialist consultation was not considered necessary.

The occurrence of signs originating from the central nervous system soon after the injection of a vaccine may be explained in several ways. There may be a true causal relationship ; but the matter may also be due to pure coincidence, since it is well known that a considerable number of infants (certainly 1 : 500 or more) aged 3 to 6 months show neurological signs without ever having been immunized. A true causal relationship can only be explained by the release of a trigger mechanism in an individual in some way predisposed to neurological illness, because the overwhelming majority of children never show serious nervous signs after receiving injections of the same vaccine. The predisposition may be of greatly varying nature: it may be congenital or acquired, permanent or transient, clinically manifest or latent.

The series which Dr. Ström has now published was first presented as a paper read at a meeting of the Swedish Medical Association's sections for acute infectious diseases and for paediatrics and school hygiene in 1959. It evoked lively discussion, and several speakers took a severely critical attitude to Dr. Ström's investigation and interpretation of the

findings. The Royal Medical Board later appointed a special committee to examine this investigation. Some brief excerpts of the committee's report, completed in February, 1960, follow.

"The possibility that such severe and comparatively common complications may occur is disturbing, and urgently prompts the greatest vigilance with regard to vaccination."

"Among many of the children that have shown neurological sequelae, the connexion with vaccination is doubtful or improbable."

". . . some connexion with vaccination is highly probable in . . . four cases of a series collected over a period of four years, during which time about 250,000 children may be assumed to have been immunized . . ." One case, the report adds, may possibly be added to this sum. The report continues, "A striking accumulation of cases during the period October to December, 1957, was noted with regard to those showing the greatest likelihood of a casual relationship to vaccination. The question then arises of whether the clinical signs may not have had some basic cause other than the vaccination, but with the injection as precipitating factor."

It is undeniable that vaccines may produce grave and even fatal involvement of the central nervous system. Pertussis vaccine has been incriminated oftener than other bacterial vaccines. In the noted investigations published by the British Medical Research Council in 1956[1] and 1959[2] about 46,000 children were closely watched during the month immediately following each injection of pertussis vaccine. 57 had their first convulsion within 28 days of the injection. In fact this is no more than what may be anticipated without vaccination. The time-relationship, however, indicates that the injection probably triggered off the reaction in some of the cases: 14 of the children had a convulsion within 72 hours of injection. Of the 57, 18 had at least one more convulsion, but nevertheless "all seemed fit when visited a year after the last inoculation."

The total incidence of nervous complications which Dr. Ström reports to have occurred within "up to five and seven days" is 1:6,000. The British Medical Research Council's figure for convulsions taking place within three days is 1:3,500. The essential difference between the two is to be sought in the degree of severity of the signs. No grounds for suspecting encephalopathy were considered to exist in any case in the British series. If we from Dr. Ström's results calculate the incidence of permanent damage to the central nervous system we arrive at the figure 1:16,000, and even this must be regarded as misleadingly high. After careful scrutiny of the series the special committee (whose report is quoted above) concluded the proved incidence to be 1:50,000. It should also be pointed out that some cases might conceivably have been avoided if elementary precautions had been taken (several children received second or third injections even though a previous injection had produced transient threats of central nervous damage).

Everything should be done to reduce the risk of side-effects of immunization. With regard to grave complications, every individual, convincingly documented case is a serious encumbrance. We do not deny that Dr. Ström's findings give reasons for serious thought, but we do hold that in such an important connexion every case should be scrutinized in detail before it is accepted as constituting a "neurological complication to vaccination." The two clinicians among us (B.V., R.Z.) have seen patients in whom subsequent investigation disclosed that a grave cerebral lesion had undoubtedly existed before vaccination was undertaken (birth injury, congenital anomalies, infantile spasms, degenerative disease). A constructive attitude to the whole problem of vaccination is essential. This implies collaboration between clinicians and manufacturers of vaccines, precise directions to doctors and nurses concerning technique of injection and contraindications, and constant consideration of the most appropriate disposition of the vaccination programme.—We are, etc.,

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Department of Paediatrics, Gothenburg University. R. ZETTERSTRÖM.

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[1] *Brit. med. J.*, 1956, 2, 454.
[2] Ibid., 1959, 1, 994.

Radio Doctor

SIR,—Can someone please ask the radio doctor to be a little more considerate? On November 30, having told the public that a stye on the eye was a comparatively trivial matter, he said, "Go to your doctor for an antibiotic." Now antibiotics are expensive and are all too often misused, as he must well know. A doctor is annoyed if a patient comes demanding a certain form of treatment, and the patient is annoyed if he does not get it—annoyance all round.

Perhaps the R.D. is not a G.P. or he would understand.—I am, etc.,

Eastbourne, Sussex. E. VENN CLAYDON.

SIR,—In a B.B.C. programme on November 30 entitled "To-day" a doctor gave a talk on styes. He gave two pieces of advice. First, to leave the eye alone *and go to the doctor for an antibiotic*; and, second, not only not to use golden eye ointment, but to throw it away.

Nowadays people tend to accept whatever is printed or broadcast as "official," and it is unfortunate that the B.B.C. is wasting good opportunities in teaching by giving such absurd advice. Can nothing be done to guide the B.B.C. before the programmes are broadcast? We can protest afterwards, but the damage is done.—I am, etc.,

Bishop's Castle, Shropshire. G. ST. JOHN PENNEY.

Service Overseas

SIR,—The letter of Dr. Hugh B. L. Russell (October 29, p. 1313) deserves comment. All of what he has said has been said before *ad nauseam*. The backbone of British medicine overseas in the underdeveloped countries of what was formerly the British Colonial Empire has been the career officer. Unless long-term service can be maintained in the future as in the past, then British medical influence will continue to decline. Short-term contracts are not the answer. Unless something is done quickly there may be no British doctors left in East Africa in two years' time other than missionaries.

The fault lies with both the Colonial Office and the United Kingdom medical profession. The Colonial Office has repeatedly failed to produce proper guarantees, and in spite of a recent White Paper,[1 2] produced after much bludgeoning, these guarantees are not